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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,277	02/22/2005	Gavin Paul Vinson	133088.00301(P33791US)	6075

35151 7590 11/09/2010

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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
11/09/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,277	VINSON ET AL.	
	Examiner	Art Unit	
	LEI YAO	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,14,18-21,25-28 and 31-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *12,19,26 and 28* is/are allowed.

6)☒ Claim(s) *14,18,20,21,25,27,28 and 31-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/20/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed on 8/23/2019 in response to the previous Non-Final Office Action (5/21/2010) is acknowledged and has been entered.

Claims 33-36 are added.

Claims 1-11, 13, 15-17, 22-24, and 29-30 have been cancelled.

Claims 12, 14, 18-21, 25-28, and 31-36 are pending and are under consideration for a composition comprising or consisiting of the peptide of SEQ ID NO:1 and a mehtod of treating cancer or proliferative disease with an monoclonal antibody to a protein comprising the peptide.

The following office action contains NEW GROUNDS of rejection-based on newly added claims in the amendment.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 10/20/2010 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

Rejection/Objection Withdrawn

The objection of claims 19 and 26 to as being dependent upon rejected base claims 14 and 21 respectively is withdrawn in view of the amendment to the claims.

The rejection of claims 29-30 under 35 U.S.C. 102b) as being anticipated by Vinson et al (US Patent 6063620, issued 2000) is moot in view of cancellation of the claims

Rejection Maintained and Response to Arguments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14, 18, 20-21, 25, 27, 31-32 remain rejected under 35 U.S.C. 102(b) as being anticipated by Burmer et al (WO200261087, published Aug 8, 2002) as evidenced by the sequence search result-Burmer.

Response to Applicant's argument:

Applicant argues that Burmer reference does not provide an enabling disclosure of a method of treating cancer of claim 14 or smooth muscle cell proliferation of claim 21. Burmer reports a large number of sequences and list of diseases and just explains how to raise antibodies against such sequences. Burmer does not actually teach the production of any antibodies. Burmer does not provide any evidence that confirms this could be done.

Applicant's arguments have not been found persuasive for the following reasons: Burmer reference does list numbers of diseases, but all are cell growth related or regeneration-related diseases that have abnormal expression of G-coupled receptor proteins including the claimed protein. Treating cell growth related disease would

comprise treating cancer of claim 14 and cell proliferation of claim 21. The active step is administration of an antibody binding to a peptide comprising the sequence of SEQ ID NO: 1 to a subject, which may or may not have a cancer (claim 14) and smooth muscle cell proliferation disorder (claim 21) as the claims are as currently construed. Burmer at page 55-57 discloses a method of administering an antibody binding to the protein comprising the peptide of SEQ ID NO: 1, which is the same active step used in the claimed method, therefore would anticipate the claimed invention. Burmer further teach a family of G-protein couple receptors or fragments thereof. They are functionally and structurally related proteins, in which one protein comprises the instant SEQ ID NO: 1. Making antibody to a known protein is well established and commonly used technology in the field as described in the Burmer reference. Actually, Burmer clearly teach methods of making and using antibody for detecting protein and treating a disease that have abnormal expression of the protein as set forth in the rejection. Thus, Burmer teaches each and every limitation of the claims, therefore the rejection is maintained.

The following is a New Ground of rejection-based on the newly added claims

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement: treating cancer a proliferative disease with an antibody to the variant of SEQ ID NO: 1 or 2.

*Applicant is noted that the newly added claims **33-36** encompass the same scope of previously presented claims, e.g. claims 21 and 24 filed on 8/6/2008. The following rejection is reinstated the Office action set forth 12/4/2008 with modification. All the references in the rejection have been provided in the previous Office action.*

Claims 33-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating cancer or proliferative disease comprising the administration of an antibody directed against the sequence of SEQ ID No: 1 or 2 only, does not reasonably provide enablement for the full scope of the claimed methods of treating cancer or disease comprising the administration of an antibody against a conservative substitution of SEQ ID No: 1 or 2, as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factor considered when determining if the disclosure satisfies the enablement requirement and whether any is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of necessary experimentation claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re wands,* 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir.1988).

The claims are broadly drawn to a method of treating cancer or proliferative disease comprising administering an antibody to a conservative variant of SEQ ID NO: 1 and 2 having the sequence below (claims 33 and 35), wherein each of the amino

acids in SEQ ID NO: 2 could be replaced by a conservative amino acid (claims 34 and 36).

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1       8           17                                  45
MILNSSTEDGIKRIQDDCPKAGRHNYIFVMIPTLYSIIFVVGIFG   SEQ ID NO: 1
        EDGIKRIQDD                              SEQ ID NO: 2
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To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provides an enabling disclosure of how to make and use a claimed invention. The method objective of claims is treating a cancer with an antibody to a conservative variant of SEQ ID NO: 1 or 2. Thus, it would be expected that one of skill in the art would be able to use the method as claimed without undue a quantity of experimentations.

The specification teaches the peptides of SEQ ID NO: 1 and 2 that are fragments of angiotensin II type 1 receptor (page 2 and 11) and method of making a monoclonal antibody 6313 with peptide of SEQ ID NO: 2 as an immunogen. The specification teaches a method of inhibiting cancer cell including breast and prostate cell proliferation and invasion with monoclonal antibody 6313 (examples). The specification although lists conservative amino acid that can be used for substitutions of the peptide (page 4), but no antibody to the substitution variants was made and no binding of the antibody 6313 to the variants was tested.

One cannot extrapolate the teachings of the specification to the claimed invention, because the specification fails to teach what substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed, and further to allow a monoclonal antibody to bind with the retained specificity and be used in the method of treating a cancer

It is also well known in the art that for a monoclonal antibody to bind to a protein sequence, the protein sequence must maintain a strict sequence and or binding structure. For example, Coleman et al (Research in Immunology, 1994; 145(1): 33-36) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza et al (Journal of Protein Chemistry, Vol. 11, No. 5, 1992, pages 433-444) teach single amino acid substitutions outside the antigenic site on a protein affects antibody binding. These references demonstrate that even a single amino acid alteration or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristics of a binding protein or antibody.

The specification as filed has failed to provide those of skill in the art with any guidance as to which amino acids can be altered and yet maintain monoclonal antibody binding specificity. Therefore in the absence of this evidence those of skill in the art would be forced into undue experimentation to practice the invention within the full scope of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquires set forth in Graham V. john Deere Co., 383 U.S. 1, 148 USPQ 459 (1996), that are applied for establishing a background for determining obviousness under 25 U.S. 103 (a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burmer et al (WO200261087, published Aug 8, 2002) in view of Vinson et al (US Patent 6063620, issued 2000). Both references are provided in the previous Office action.

The claims are examined to a method of using antibody to the peptide of SEQ ID NO: 2.

The claims are drawn to a method of treating cancer or proliferative disease comprising administering an antibody to the peptide consisting of SEQ ID NO: 2.

The teachings of Burmer et al on the protein of a peptide comprising SEQ ID NO: 1 (45 aa) that comprises the SEQ ID NO: 2 (10 aa) have been set forth in the previous Office action and responses above. Specifically in this rejection, Burmer et al teach antibodies to the peptide or protein (page 37+) and a method of treating a cancer comprising breast or prostate cancer and disease condition associated with vascular

smooth muscle cell proliferation including atherosclerosis by administering an antibody or the fragment thereof that binds to a peptide or protein comprising the SEQ ID NO: 1 and 2 (page 56-58).

Burmer et al do not teach a peptide consisting of the sequence of SEQ ID NO: 2 (EDGIKRIQDD) and do not teach antibody specific to the peptide of SEQ ID NO: 2.

Vinson et al teach Angiotensin II type I receptor (page 1, line 50+) that is the same protein taught by Burmer et al above. Vinson et al teach a 10 amino acid peptide of the receptor that is identical to the peptide of SEQ ID NO: 2 as sequence alignment (provided in previous office action) and teach that the peptide is a conserved fragment of angiostatin II type 1 receptor cross the species, which is expressed and involved in cell vascularization and newly tissue development (page 2, line 40 and page 1, line 37+). Vinson et al teach monoclonal antibody made by the peptide as an immunogen. Vinson et al teach and suggest a method of using the monoclonal antibody for diagnosis or therapeutic applications by controlling the receptor activity (col 3, line 50). 1

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8           17                                      45
       MILNSSTEDGIKRIQDDCPKAGRHNYIFVMIPTLYSIIFVVGIFG    SEQ ID NO: 1
                 EDGIKRIQDD                             SEQ ID NO: 2
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It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the antibody of Vinson for the antibody in Burmer's method to treat a cancer or proliferative disease with expected result. One of ordinary skill in the art at the time the invention was made would have been motivated to use the Vinson's antibody in order to benefit a cancer treatment because Vinson et al have shown the peptide of SEQ ID NO: 2 is conserved sequence for the activity of angiostatin II receptor and suggest that antibody is used for therapeutic application and Burmer et al have shown a method of treating a cancer with antibody to the receptor. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for combining the teachings

to treat cancer because Burmer et al have taught a method of treating cancer with an antibody to the entire protein and Vinson et al have made and used the antibody to block the activity of the receptor. Therefore, the references in combination teach every limitation of the claims and the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Conclusion

Claims 12, 19, 26 and 28 are allowed. Claims 14, 18, 20-21, 25, 27, and 31-36 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on 571-272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao/
Examiner, Art Unit 1642

/Misook Yu/
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